

THE INFLUENCE OF FOOD ON THE ENDOGENOUS
URIC ACID EXCRETION IN MAN

BY

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I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY
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INTRODUCTION

Since the discovery of uric acid in urinary calculi by Scheele (1) in 1776, the study of its role in vital processes has been of increasing interest and primary importance, not only for theoretical reasons as to the manner of its formation, circulation, and elimination in the animal body, but also because many pathological conditions are known to be accompanied by changes in the concentration of this purine in blood, tissues and urine.

Despite the mass of literature compiled in the investigation of the many problems related to uric acid(2), a large part of the evidence obtained has been contradictory and logical conclusions impossible, while experimental data have been in many cases unreliable because accurate methods for the determination of small amounts of uric acid have not been available until recently. Also the need for the proper control of experiments with regard to such factors as food and water intake and the like has not been clearly recognized in the past. Benedict(2) has recently said in commenting on Mendel's statement in 1906, "We assuredly need to know more about the origin and significance of endogenous uric acid," that it is a sad commentary upon progress of ten years that it becomes necessary to modify Mendel's statement and say, "We want assuredly to know something about the origin and significance of endogenous uric acid".

It is generally recognized that uric acid, among the most important of the nitrogenous excretions of man, does not arise from the metabolism of simple protein, but takes its origin from

the nucleic acids of the nucleoproteins of food and tissues. The studies of Marč in 1887(3), Burian and Schur in 1900(4) and others (5) have shown that the nucleins of the diet decompose directly, giving rise to the exogenous fraction, while the uric acid eliminated during fasting or on a purine-free diet is to be regarded as endogenous in its origin(6). Endogenous uric acid may originate from the activity of micro-organisms of the alimentary tract(7) as well as from the tissues of the body, and some small part may be due to the disintegration of white blood corpuscles, although the leucocytosis theory of Horbaczewski(8) that uric acid excretion is a measure of the degree of this decomposition is not now tenable. The view of Weintraud(9) that all food must become a part of living tissue before it is metabolized has little experimental basis. An exact knowledge of the sources of uric acid is complicated by the possibility that the amount eliminated may be only a part of that formed, since even in man, the possibility of a small amount being oxidized by the organism to allantoin(10), to urea(11), or to other substances(12) has not been entirely excluded. It is not impossible that the decomposition products themselves or certain complexes of the protein molecule(13) may reunite to form the original purines

The spleen(14) has been held by many investigators to bear a close relation to uric acid formation because of its richness in leucocytes and nucleins. However, experiments by Mendel and Jackson(15) show no changes in uric acid excretion after spleenectomy. The liver(16) also has been regarded as the organ responsible for uric acid formation, but Lieblein(17) has shown that there is no marked decrease in uric acid excretion in cirr-

hosis, in hypertrophy of the liver, or in artificially produced hepatic degeneration, while Hahn and Nencki(18) have shown by the use of an Eck fistula that uric acid is not increased under this condition. Thus our present knowledge will not permit us to assign the function of uric acid formation to any particular organ or group of organs.

Because of its insolubility uric acid does not circulate in the body as such. Most of the earlier workers held that it existed normally in body fluids as sodium biurate or quadriurate. It is now considered to be held in solution in the urine by urea and disodium hydrogen phosphate(19). The question of the solubility of urates and their deposition in the tissues and joints becomes one of great importance pathologically, in connection with such diseases as arthritis, nephritis, acute febrile conditions, lobar pneumonia and particularly gout. The exact role which uric acid plays in an acute attack of gout is still an open question, while it is not known whether the deposition in the joints produces the disease or results from it. Chief among the many different methods for the treatment of gout is the administration of substances intended to dissolve the local deposits of uric acid in the joints. The substances which have been most widely used are sodium salicylate, piperazine, lysidine, lithium salts and sodium benzoate, although at present atophan is rapidly replacing these as a therapeutic agent. The data are so conflicting, however, that no conclusion of value can be drawn from them. There can be no intelligent treatment of the diseases in which uric acid is a causative or contributory factor until the facts concerning its role in normal

physiological processes are more clearly understood. That ingestion of purine-free food, particularly protein food, leads to a rise in the excretion of endogenous uric acid has been recognized for many years(20). The cause of this increase in the endogenous uric acid excretion has been the subject of much controversy(21). The most widely accepted view holds that glandular activity especially that of the digestive glands is responsible for the formation of the endogenous uric acid. The evidence upon which this theory is based(21), however, seemed insufficient, and with this in mind the present study was undertaken. The purpose of the experiments was to study the effect produced upon endogenous uric acid excretion by various foodstuffs and chemical substances and to determine as far as possible what factors are responsible for the variations in the endogenous metabolism of this purine.

EXPERIMENTAL

Technique

Methods Uric acid was determined colorimetrically by the Benedict and Hitchcock modification of the Folin-Macallum-Denis method. Creatinine was determined by Folin's micro-colorimetric method and total nitrogen by Kjeldahl method.

The subject of the experiments was a healthy young man aged 22 years, weight about 58 kilos. During a period of over 6 months from September 25, 1917 to April 1, 1918, a meat-free low protein diet, which may be considered as a "purine-free" diet was consumed with the exception of a few meals during the holidays at which meat was taken. Under these dietary conditions the endogenous uric acid excretion was maintained at a minimum, ^{although} no attempt was made to maintain a quantitative uniformity in the diet. During the experimental periods, no food was eaten from 6 P.M. the preceding day until the completion of the experiment. Thus any rises in the uric acid output may be attributed to the influence of the particular substance ingested.

Some of the recent experiments in which the hourly excretion of uric acid was studied(21) are open to the criticism that the volumes of urine collected are low, frequently falling below 20 cc. Under such conditions manipulative errors would be more significant than with larger volumes of urine. In the present investigation the Benedict-Hitchcock colorimetric method was found to be both convenient and accurate for the determination of

small amounts of uric acid. In order that errors arising from manipulation or from incomplete emptying of the bladder might be kept percentagely as low as possible, it was though desirable to maintain an average hourly volume of urine of at least 100 cc. by the ingestion of 200 cc. of water at the beginning of each hourly period. Hourly determinations of creatinine were also made on the samples. As creatinine is uninfluenced by diet and tends to maintain a constant hourly level, it was believed that any marked variation from the normal creatinine level in any period would indicate incomplete collection of the urine.

The samples were preserved with chloroform in tightly stoppered bottles until the routine analyses could be carried out. In the majority of the experiments the uric acid determinations were finished on the experimental day. Creatinine was usually determined the following day, although in a few cases this was impossible.

Fasting Control Experiments

(Tables I and II)

If changes in the excretion of uric acid following ingestion of food and other substances are to have any significance, it is necessary to have accurate information concerning the degree and kind of variations to be expected in the fasting subject normally. Control experiments in which no food was ingested throughout the period covered by the experiments were carried out and repeated at frequent intervals in order to secure evidence that the level of endogenous metabolism was not altered by the long continued purine-free diet. Protocols of such experiments are given in

Tables I and II. In each of the control experiments there was exhibited a tendency toward a fall in the excretion near the end of the experimental period. This is in accord with the observations of Mendel and Stehle(21) and of Neuwirth(22). The controls were remarkably constant throughout all the experiments, the hourly variations being less marked than those observed by the above mentioned investigators.

On the basis of these normal days, it does not seem unreasonable to assume that a rise in uric acid excretion above 25 mg. in any one hour or hours, following the ingestion of some substance is the result of the action of this substance. It is not considered that a rise of a few milligrams has any special significance.

In Table I are also recorded normal creatinine and total nitrogen figures. The amounts of creatinine excreted are constant within experimental limits and are typical of the results obtained in other experiments. While there is a relative constancy in creatinine excretion in any one experiment, it would seem from some of the data obtained that the level does not remain absolutely constant. No relation between diuresis and uric acid excretion or between total nitrogen and uric acid was apparent(cf. Neuwirth (22)).

It should be noted also here that two control experiments were carried out, although not included in these tables, in which the endogenous excretion was nearly double that shown in other experiments, averaging about 30 mg. per hour and remaining at this high level throughout the day. These were obviously not

representative days and were due to some unexplained abnormality. These experiments are discussed also under exercise in a later part of this paper. These data serve to illustrate the necessity of frequent carefully conducted control experiments.

Protein and Protein Derivatives

(Tables III - XIII)

Protein It has repeatedly been shown that the excretion of endogenous uric acid is increased by purine-free protein food(20)(21). The experiments recorded in Table III, IV and V are in agreement with previous work. After ingestion of each type of protein food, cottage cheese, glidine*, and egg white, there occurs a rise in

* Glidine is a commercial diabetic flour. The preparation used in these experiments contained 15.1 per cent N, equivalent to 94 per cent protein.

uric acid excretion clearly above the basal level, a rise which usually attains its maximum height during the third or fourth hour after administration of the protein. The two experiments with glidine (Table V) show some sort of a quantitative relationship for in Experiment 32, 66.6 gms. of glidine increased the excretion much more markedly than did one half that amount (Exp. 31). It was not possible to continue experiment 32 long enough to determine whether the maximum effect had been reached. No clearly defined quantitative differences between three types of protein in regard to their effect on the uric acid excretion could be observed.

Hydrolysis Products of Protein Digestion - Amino Acids -

In order to test the validity of the theory that rises

in endogenous uric acid after ingestion of protein result from the wear and tear on the glandular tissue occasioned by the work of digestion(21), the amino acids, alanine, glycocoll, glutamic acid, aspartic acid and the amide, asparagine were taken. It is evident from Table VI to IX, that these substances, representing the final products of protein digestion stimulate the formation of endogenous uric acid, in a manner similar to proteins themselves, although the effect is produced sooner and is more marked. The results of successive doses of glycocoll on the same experimental day (Table X) seem to leave no doubt as to the effect of the amino acids, since after the usual increased excretion and return to normal following a dose of glycocoll, another increase similar in all respects to the first was obtained with a second dose of glycocoll. This experiment also shows clearly that the rises in uric acid excretion following amino acid ingestion are not the result of a removal of preformed uric acid or uric acid precursors from the tissues, since in that case it seems probable that the first administration of glycocoll would force out the reserve store and the second dose be without influence. However, the results are the same in both case so that the effect would seem to be due to increased uric acid formation rather than to an exaggerated elimination of purine reserve stored.

It might be considered that the factors of diuresis(22), and of nausea which was quite severe after the ingestion of the dicarboxylic acids, glutamic and aspartic, were instrumental in increasing the uric acid output, but a study of Table IX shows that there is no basis for this supposition. During the hour

the first thing I noticed when I stepped out of the car was the
familiarity of the air. It felt like I had been here before, like I
had been in the arms of a friend. The sun was shining brightly, and
the birds were singing. It was a beautiful day, and I was
in the best of luck. I had found a place that was just what I
needed. It was a small, quiet town with a big heart. The people
were friendly, and the food was delicious. I had found a home.
I had found a place where I could be myself. I had found a place
where I could be happy. I had found a place where I could be
free. I had found a place where I could be me.

11-12, with the exceptionally large volume of urine of 527 cc., some 23 mg. less uric acid were eliminated than during the previous hour with a low volume of 71 cc., while the uniformity of the creatinine figures show the collection of the urine to have been complete at each hour. Asparagine which produced effects comparable in magnitude to those of the dicarboxylic amino acids, produced no nausea or other gastro-intestinal irritation which would seem to rob this of its significance as a causative factor. The asparagine experiment is also of interest as showing that masking of one carboxyl group does not alter the activity and that an amide of this type resembles the dicarboxylic acids rather than the monocarboxylic acids in its effects. This is perhaps not surprising in view of the readiness with which asparagine loses its amide group and passes to aspartic acid.

What factor is responsible for these increases? Since no digestive processes are required for the utilization of these amino acids, it can not be considered under these experimental conditions that the rises in endogenous uric acid are due to the work of the digestive glands. It is possible that the effect may be due to a direct stimulation of the body cells by the amino acids or their katabolism production^s, a stimulation of nuclear metabolism rather than general metabolism, since the creatinine excretion remains constant.

Early in these experiments it seemed very probable that there might be some relation between the stimulation of the nuclear metabolism by amino acids and their specific dynamic action, especially since glycocoll, known to exert a greater specific dy-

namic action than alanine(23) had a more marked influence on uric acid excretion than did the latter acid. But on testing out this hypothesis further, it was observed that glutamic and aspartic acids, which probably have no specific dynamic action* according

*In a recent paper Grafe(25) reports experiments which seem to indicate that the dicarboxylic amino acids have marked specific dynamic action. The experiments do not seem as well controlled as those of Lusk.

to Lusk(24) increased the elimination of endogenous uric acid more markedly than either alanine or glycocoll. From these results it would seem that the specific dynamic action of protein and amino acids bears no direct relation to their influence on nuclear metabolism.

Sarcosine If the stimulating influence on nuclear metabolism, common to at least four amino acids, is inherently a property of amino acids as such, it seems probable that substituted amino acids would exhibit a similar influence. If, on the other hand, the activity is due, ^{to} not the amino acids as such, but to their katabolic products, a substituted amino acid which does not follow the normal path of amino acid catabolism would in all probability exert no such influence. Sarcosine, methyl glycocoll, was chosen to test this hypothesis, since it has been found to pass unchanged through the body for the most part(26), although a small amount may be converted to methyl hydantoic acid(27) or creatine.

The elimination of uric acid after sarcosine ingestion (Table XI), shows a slight rise at 10 A.M. to 23.9 mg. However,

a normal hour from 7 to 8 A.M. shows a rise to approximately the same height, so that a true increase has probably not occurred as a result of the sarcosine ingestion. In any case the effect is too slight to be significant or comparable to that produced by the other amino acids. Because of the inability to obtain more sarcosine, this experiment could not be repeated. From this one trial it would appear that the stimulation of purine metabolism is not a property of amino acids as such.

Ammonium Chloride In order to further study what group or reaction is responsible for the effects of protein and amino acids on uric acid metabolism, an investigation of the influence of products of protein katabolism was planned. Since the first step in amino acid katabolism within the body is deaminization, the influence of ammonia was next studied. The ammonia was administered as the chloride, which is less toxic than most other ammonium compounds. Inorganic ammonium salts are not converted to urea(28), so that the compound chosen should show whether ammonia as such is the factor influencing the changes in purine metabolism observed.

The figures given in Table XII show that no rise of uric acid excretion above the normal has occurred. This is direct evidence that free ammonia from the deaminization of amino acids, plays no role in stimulating the production of endogenous uric acid.

At this point, it would have been logical to have studied the effect of ammonium carbonate, citrate, or some other organic ammonium salt, which is capable of further transformation in the organism to form urea. Such an experiment should show whether the conversion of ammonia to urea, is a factor related to the stim-

ulation of endogenous uric acid formation. Because of their toxicity in doses comparable to those administered as amino acids, experiments with this type of ammonium salts were not carried out.

Urea Since ammonia does not seem to exert any influence on the uric acid excretion, the next step, logically, should be to determine the effect, if any, of urea, the end product of the katabolism of the nitrogenous part of the amino acid molecule. As shown in Table XIII, the excretion of uric acid following ingestion of urea does not vary appreciably from the normal. Urea is therefore probably not responsible for the rises in uric acid excretion after ingestion of amino acids.

Non-Nitrogenous Rest Since it is improbable that the nitrogenous rest of amino acids is the factor which determines their stimulating effect on endogenous purine metabolism, the influence might in some way result from the activity of the non-nitrogenous rest. It is not easy to test experimentally the influence of this portion of the amino acid, since the various α - ketonic acids, supposed to be formed in the intermediary metabolism are very toxic in large doses. Although there is uncertainty concerning the products of intermediary metabolism of amino acids, it is believed that in the case of many, the non-nitrogenous rest may be finally converted to glucose. This suggested the possibility that glucose might be the factor responsible and experiments were carried out with this and other sugars, since direct experiments upon the non-nitrogenous rest seemed impossible.

Carbohydrates

(Tables XIV - XVI)

Glucose The results of the ingestion of 100 gms. of glucose (Table XV) show no indications of a rise in uric acid excretion above the normal fasting level*. Glucose is clearly not the de-

*Other experiments carried out by Mr. E. A. Doisy in this laboratory have shown that 200 gms. of glucose also have no effect on uric acid elimination.

termining factor.

Disaccharides - Sucrose and Lactose

Additional experiments with large amounts of sucrose and lactose were performed. The results of these experiments are given in Tables XV and XVI and are clearly negative as far as changes in the uric acid elimination are concerned. This is not in harmony with the results of Mendel and Stehle on sucrose(21).

Fats

(Tables XVII and XVIII)

Butter In order to study the effect of foodstuffs other than protein and carbohydrate, two experiments in which 100 grams of butter were fed were carried out (Table XVII). In both experiments slight rises in uric acid excretion were observed the third and fourth hours following ingestion. These results are not in harmony with those obtained by Mendel and Stehle(21) or by Doisy in this laboratory previously(29).

Glycerol In view of the results obtained with butter, it was considered that the effects observed might be due to the glycerol lib-

erated on saponification of the butter fat. Glycerol if not recombined into fat during absorption may be converted into glucose in the organism. The work of metabolism of glycerol might be responsible for the slight rises observed. It should be borne in mind that the amounts of glycerol combined in 100 gms. fat are not large. The experiments with glycerol (Table XVIII) show that it produces a distinct rise in endogenous uric acid excretion, a rise lasting for a period of several hours. Similar results although much less marked, have been obtained by other investigators(30), although the plan of the experiments was so different as to make the results hardly comparable with those of the present series. The rise from 10 gms. glycerol, Exp. 40, an amount comparable to that present in 100 gms. fat is less marked, being hardly above the experimental variation of the controls.

Exercise

(Table XIX)

The experiments carried out to determine the influence of exercise upon the excretion of endogenous uric acid are not an integral part of the present study. They were performed mainly in an endeavor to establish the cause of the abnormality of the two control experiments already referred to. The normals in question showed an elimination of uric acid of nearly 30 mg. for each of the first four hours of the day. Since there seemed to be no other factor to which this abnormal elimination might be ascribed, it was thought possible that some rather strenuous exercise, taken in each case two days previously, might be responsible. Many investigators(31) have recorded rises in uric acid excretion following

exercise, while others find no effect(32). The results of the one experiment in Table XIX are negative. The exercise taken was of an hour's duration, but was exhaustive and if truly operative in influencing uric acid excretion, presumably results from analysis of the urine immediately following the exercise, should be positive, but as stated no effects were noted. The low excretion from 9-10 in Exp. 26 is probably due to incomplete elimination as is indicated by the creatinine elimination and the figures for the following hour. Many more carefully controlled experiments are necessary before conclusions can be drawn as to the influence of exercise.

GENERAL DISCUSSION OF RESULTS

The outstanding fact in our knowledge concerning endogenous uric acid, is that protein increases the output of this purine above the amount normally eliminated during fasting. Since no nuclear material is present in the food, this extra uric acid can not have an exogenous origin and must arise either as a result of the work of the digestive glands during the digestive processes or from a direct stimulation of nuclear metabolism by the products of digestion of proteins. The former possibility seems plausible enough and is usually given as the probable explanation, although there is little clear-cut experimental evidence upon which to base an assumption of this sort.

The most convincing experiments in favor of the theory that work of the digestive glands is involved in the stimulation of nuclear metabolism have been furnished by Mendel and Stehle(21). The conclusions of these investigators are based largely upon results secured from pilocarpine and atropine ingestion. These two drugs act antagonistically, the former increasing and the latter depressing secretory activity. It is very striking indeed that the ingestion of these two drugs should increase and decrease respectively in so remarkable a manner the uric acid output, as is shown by the experiments referred to. If it be true that the functional activity of these drugs be a stimulation and inhibition of the nerve endings of the secretory glands alone, there can be no hesitation in accepting the conclusions as to the role of the work of digestion, which naturally follow from these experiments.

However the experiments of the present series furnish positive evidence that the power of stimulating endogenous uric acid elimination is not limited to protein alone, since amino acids the final products of proteolysis, give rises even more pronounced. This indicates that the digestive factor is not, at least, the main factor responsible for the increased formation of uric acid. Furthermore Mathews has shown in experiments upon star-fish(33) that the drugs atropine and pilocarpine act directly on many types of cells and that their action is not confined to the secretory nerve ends. The effects of these drugs are probably due to a stimulation and inhibition of the oxidative processes occurring within the cells and are not confined merely to the nerve endings of the secretory glands. Consequently the hypothesis that protein taken into the alimentary tract causes increased functioning of the digestive glands which in turn gives rise to stimulation of endogenous uric acid production, is not necessarily the only tenable one. It is more probable that pilocarpine and atropine act typically as stimulants or depressants on the oxidative processes of many types of body cells, resulting in increased metabolism of nuclear material.

One other objection to the theory of digestive work as a stimulus does not seem to have been considered sufficiently hitherto. If the work of the digestive glands is the main contributing factor, why does not ingestion of carbohydrates and fats cause rises similar to protein? There is no evidence that protein imposes more of a strain on the digestive mechanism than do the other foodstuffs. How can the difference be explained?

The experiments of the present series seem to emphasize rather the role of the amino acids in protein, known to be more active in stimulating metabolism, than are the fats or sugars, as stimulants of nuclear metabolism. Proteins and amino acids stimulate this function, but not urea, ammonia, or glucose. The most probable explanation of the action of proteins seems to be in the stimulus to cell processes from the non-nitrogenous portions of the amino acid molecule, or their intermediary products. These have been shown by Lusk to be responsible for the specific dynamic action of amino acids(23).

The following hypothesis is put forward tentatively to account for the rises in uric acid elimination occasioned by the ingestion of non-nuclear food. Variations in endogenous uric acid are probably due to a direct and specific stimulation or inhibition of the normal processes of body cells resulting in increased nuclear metabolism.

SUMMARY

I. The following substances increase the excretion of endogenous uric acid in the fasting subject, viz: egg white, gli-dine, cottage chesse, alanine, glycocoll, glutamic acid, aspartic acid, asparagine, butter, and glycerol. The effect of the last two is less marked than of the others.

II. Sarcosine, ammonium chloride, urea, glucose, sucrose, and lactose when ingested are without appreciable effect upon the endogenous uric acid metabolism.

III. There is no necessary relation between the specific dynamic action of foodstuffs and their activity in stimulating nuclear metabolism.

IV. Increased uric acid production of endogenous origin, by foodstuffs seems to be the result of a specific stimulus. The effect is probably not due to protein as such, amino acids, the ammonia liberated by deaminization, nor to the urea, the end product, but to some intermediary product originating from the non-nitrogenous rest.

V. The bearing of the experimental facts of the present study upon the theory that increased nuclear metabolism is mainly due to the work of digestion is discussed. From the data here presented, this theory seems no longer tenable. The following tentative hypothesis is proposed. Variations in endogenous uric acid excretion following ingestion of food are due to a direct and specific stimulation or inhibition of normal processes of body cells

The first of these is the fact that the theory is not a simple statement of the facts, but a statement of the facts as they are interpreted. The second is the fact that the theory is not a simple statement of the facts, but a statement of the facts as they are interpreted. The third is the fact that the theory is not a simple statement of the facts, but a statement of the facts as they are interpreted.

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resulting in increased nuclear metabolism.

VI. The influence of exercise on endogenous purine metabolism is discussed.



Table I

Experiment 3 - Fasting Normal

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
6-7	122	20.7	61.0	386.7
7-8	210	19.9	58.8	425.8
8-9	291	18.5	64.2	416.1
9-10	150	15.0	63.0	355.5
10-11	92	16.5	59.8	345.0
11-12	122	15.5	59.7	339.1
12-1	311	17.1	62.2	441.6

Table II

Experiments 2,7,19,24 - Fasting Normals

200 cc. water per hour

Ex. 2

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg
6-7	42	18.3
7-8	220	19.3
8-9	283	21.8
9-10	88	14.9
10-11	132	13.2
11-12	59	15.3
12-1	214	14.1

Ex. 7

<u>Volume</u> cc	<u>Uric Acid</u> mg
68	21.7
160	16.8
176	17.6
260	15.1
296	16.7
120	18.9
222	14.4

Ex. 19

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg
6-7	63	16.9
7-8	274	14.8
8-9	167	17.5
9-10	136	15.4
10-11	286	17.7
11-12	110	14.6
12-1	196	13.4

Ex. 24

<u>Volume</u> cc	<u>Uric Acid</u> mg
48	17.4
98	18.4
65	19.7
110	16.2
51	14.3
241	15.2
79	17.7

Table III

Experiment 4, 39 - Protein - Egg White

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Experiment 4</u>	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
		<u>Uric Acid</u> mg		
6-7	136	21.7	58.6	484.1
7-8	273	21.8	57.3	455.4
8-9 ¹	245	23.5	58.8	443.4
9-10	244	24.4	58.5	470.6
10-11	166	28.2	58.1	489.7
11-12	75	29.2	57.7	453.0
12-1	332	19.9	59.2	574.3

Experiment 39

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	18	16.0	58.8
7-8	48	21.1	54.5
8-9 ²	194	24.2	54.9
9-10	219	24.3	53.4
10-11	147	26.9	57.6
11-12	164	23.7	59.0
12-1	249	25.1	62.9

1. 300 grams egg white poached eaten at 8 A.M.
N content = 5.85 grams.
2. Poached egg white (from 16 eggs) eaten at 8 A.M.
N content = 9.3 grams.

Table IV

Experiment 12 - Protein - Cottage Cheese

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
6-7	156	19.3	56.2	429.0
7-8	207	19.8	59.2	459.5
8-9	303	20.0	58.5	478.7
9-10 ¹	58	15.2	55.7	281.5
10-11	96	24.1	62.4	579.8
11-12	96	23.2	58.5	595.2
12-1	200	18.0	56.0	628.0

1. 200 grams cottage cheese taken at 9:15.
N content = 4.8 grams (Approximately)

Table V

Experiments 31 and 32 - Protein - Glidine

200 cc. water per hour

<u>Ex. 31</u>			<u>Ex. 32</u>	
<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Volume</u> cc	<u>Uric Acid</u> mg
6-7	42	14.1		
7-8	218	17.1	51	17.5
8-9	265 ¹	16.6	245	19.2
9-10	170	23.6	268 ²	19.8
10-11	208	22.2	156	27.9
11-12	200	16.6	99	26.7
12-1	53	16.1	70	29.2

1. In Experiment 31, thirty-one and seven tenths grams of glidine were taken dry at 8:00 A.M. Glidine has an unpleasant but not nauseating taste and was rather difficult to wash down on account of its insolubility and tendency to form a paste which stuck to the mouth. No bad after effects were experienced.

2. In Experiment 32, 66.6 grams of glidine were taken at 9:00 A.M. N content = 10.1 grams.

Table VI

Experiments 6 and 10 - Amino Acids - Glycocoll

200 cc. water per hour

Experiment 6

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	80	26.4	64
7-8	185	24.0	57.3
8-9 ¹	115	36.8	59.8
9-10	142	29.8	55.4
10-11	449	22.4	56.5
11-12	77	20.1	59.2
12-1	77	14.6	58.5

Experiment 10

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	150	21.6	56.4
7-8	300	21.9	58.8
8-9 ²	117	23.4	57.3
9-10	294	30.2	57.9
10-11	210	21.2	55.8
11-12	65	19.7	53.3
12-1	166	19.4	59.7

1. 17.4 grams glycocoll eaten at 8 A.M.
N content = 3.25 grams.
2. 10.4 grams glycocoll eaten at 8 A.M.
N content = 1.94 grams.

Table VII

Experiments 8 and 23 - Amino Acids - Alanine

200 cc. water per hour

Experiment 8

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	94	19.5	56.4
7-8	231	18.5	52.2
8-9	166	24.4	58.1
9-10	257	24.4	50.8
10-11	196	23.3	56.8
11-12	110	17.6	56.1
12-1	161	16.5	60.8

Experiment 23

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	100	18.9	57.0
7-8	271	17.6	56.4
8-9	108	21.5	58.8
9-10	291	25.9	55.3
10-11	79	17.1	54.9
11-12	57	17.8	54.2
12-1	36	14.4	47.8

1. 20 grams alanine taken at 8 A.M.
N content = 3.14 grams.
2. 12.1 grams alanine taken at 8 A.M.
N content = 1.9 grams.

Table VIII

Experiment 16 - Amino Acids

Successive doses of glycocoll

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
6-7	80	19.1	58.4	401.6
7-8	229	21.5	57.7	403.0
8-9 ¹	67	24.6	59.5	300.1
9-10	244	30.7	61.0	460.7
10-11	245	20.3	59.8	421.4
11-12 ²	86	19.1	55.5	360.3
12-1	256	30.2	62.4	524.8
1-2	326	18.3	55.1	475.9
2-3	76	14.7	49.9	395.2
3-4	49	14.1	54.4	345.9

1. 10.2 grams glycocoll at 8 A.M.

N content = 1.90 grams.

2. 10.2 grams glycocoll at 11.05 A.M.

Table IX

Experiment 11 - Dicarboxylic Amino Acids -
Glutaminic Acid

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
6-7	100	18.8	55.5	368.0
7-8	293	19.1	50.9	383.6
8-9	44	27.8	54.1	219.1
9-10	40	44.4	54.0	256.0
10-11	71	46.8	54.6	394.0
11-12	527	23.7	49.7	548.0
12-1	165	19.9	47.8	396.0

Twenty grams of Kahlbaum's glutaminic, containing 1.9 grams of nitrogen, were taken at 8:00 A.M. As the glutaminic acid is quite insoluble in cold or hot water, it was necessary to add 7 grams of sodium carbonate and heat strongly in order to effect solution. This solution still reacted faintly acid and had no immediate taste, but had a disagreeable after taste which was removed in part by taking a half dozen raisens. No bad effects were experienced until 30 minutes had elapsed, at which time burning sensations were felt in the stomach, while a feeling of numbness came just above the right eye and general dizziness and nausea ensued. These symptoms gradually grew weaker during the hour, but came on with renewed vigor after taking 200 cc. of water at the beginning of the next hour. By 1:00 P.M. most of these ill effects had disappeared, but did not entirely during the whole day.

Table X

Experiments 17 and 21 - Dicarboxylic Amino Acids
and amide - Aspartic Acid and Asparagine

200 cc. water per hour

<u>Experiment 17</u> <u>Aspartic Acid</u>			
<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> Mg	<u>Creatinine</u> mg
6-7	75	17.2	56.4
7-8	310	21.5	53.0
8-9 ¹	53	22.0	53.5
9-10	37	45.2	56.9
10-11	102	29.7	57.2
11-12	42	17.7	55.3
12-1	52	16.7	50.2

<u>Experiment 21</u> <u>Asparagine</u>			
<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	162	20.2	55.1
7-8	303	22.2	60.6
8-9 ²	63	25.3	57.8
9-10	85	38.6	56.1
10-11	474	22.5	57.3
11-12	78	18.5	57.7
12-1	152	15.0	54.7

1. 18.4 grams aspartic acid taken at 8 A.M. 7 grams of Na_2CO_3 added to get acid into solution. No nausea. Diarrhoea lasting several hours. (N content = 1.9 gms)

2. 18.4 grams of asparagine containing 1.9 grams of amino nitrogen (disregarding the amide nitrogen) taken at 8 A.M. 18.4 grams went into solution quite readily in 100 cc. of boiling water, but had to be taken warm for the amide

crystalizes out at this concentration in the cold. The solution has a rather disagreeable initial taste, which was relieved by chewing gum, but no unpleasant after taste. No abnormal symptoms developed.

Table XI

Experiment 22 - Amino Acids - Sarcosine

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	31	17.4	51.4
7-8	172	24.1	63.6
8-9 ¹	168	20.3	58.8
9-10	210	23.9	61.3
10-11	317	22.3	62.7
11-12	58	17.2	53.7
12-1	30	14.1	54.5

1. 10 grams sarcosine taken at 8 A.M. N content =
1.6 grams. No ill effects.

Table XII

Experiment 18 - Ammonium Chloride

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg	<u>Nitrogen</u> mg
6-7	32	20.4	54.2	340.4
7-8	120	22.7	55.8	458.4
8-9 ¹	55	16.5	53.8	395.4
9-10	59	18.2	56.7	454.3
10-11	330	20.1	55.0	607.2
11-12	247	17.0	53.1	553.2
12-1	273	15.5	55.4	543.2

1. 7.4 grams of NH_4Cl containing 1.94 grams of nitrogen taken at 8:00 A.M. NH_4Cl was dissolved in 30 cc. of water and drunk slowly, finishing at the end of 5 minutes. It had a very salty, sharp biting, taste, but left no unpleasant after taste and produced no toxic symptoms except the following: In 15 minutes a dull pain in the stomach accompanied by slight burning sensations. in 30 minutes there was a feeling of slight nausea and a desire to vomit which desire came near a realization when one-half of the hourly portion of water was taken at 9 A.M. However, none of the NH_4Cl was lost and all of these symptoms disappeared completely by 11 A. M.

Table XIII

Experiments 14 and 15 - Urea

200 cc. water per hour

Experiment 14

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	59	18.7	61.7
7-8	229	18.3	56.1
8-9 ¹	330	17.1	58.7
9-10	127	20.6	57.5
10-11	177	22.1	60.4
11-12	177	22.1	58.9
12-1	213	13.7	57.5

Experiment 15

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7			
7-8	29	15.4	50.9
8-9	192	18.2	55.5
9-10 ²	96	20.0	56.6
10-11	260	19.5	56.1
11-12	132	16.3	50.9
12-1	209	20.0	57.7

1. 6.6 grams urea taken at 8 A.M. N content =
3.14 grams. No ill effects.
2. 6.6 grams urea taken at 9 A.M. No ill effects.

Table XIV

Experiment 36 - Carbohydrate - Monosaccharide - Glucose

200 cc. water per hour

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
7-8	21	16.8	52.5
8-9	58	22.4	58.0
9-10 ¹	55	17.4	54.2
10-11 ²	46	15.2	56.1
11-12	166	17.4	59.8
12-1	366	22.3	60.7

1. 100 grams pure glucose were taken dry at 9 A.M.
2. By means of Benedict's solution, a slight test for reducing sugar could be obtained the second hour, from 10-11, but none the first or third hours.

Table XV

Experiments 27 and 28 - Carbohydrate - Disaccharides -
Sucrose.

200 cc. water per hour

Experiment 27

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	25	16.2	50.0
7-8	36	16.1	52.1
8-9 ¹	22	19.7	55.0
9-10	20	18.3	54.4
10-11	214	20.5	57.9
11-12	190	17.7	59.1
12-1	45	15.1	53.5

Experiment 28

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7			
7-8	80	16.4	51.7
8-9	202	19.0	61.2
9-10 ²	61	15.4	53.0
10-11	89	19.0	58.5
11-12	93	17.6	55.3
12-1	160	17.9	55.5

1. 100 grams sucrose at 8 A.M.

2. 100 grams sucrose at 9 A.M.

No reduction test (Benedict's) throughout
either experiment.

Table XVI

Experiments 29 and 30 - Carbohydrate - Lactose -
Disaccharides

200 cc. water per hour

Experiment 29

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7			
7-8	65	19.9	52
8-9	243	22.6	62.9
9-10 ¹	213	19.6	58.6
10-11 ²	303	23.0	62.7
11-12 ³	103	17.6	55.0
12-1	127	19.2	61.7

Experiment 30

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	105	17.6	59.9
7-8	273	18.4	55.1
8-9 ⁴	277	17.9	60.1
9-10	252	16.1	57.4
10-11	271	16.0	58.8
11-12	106	14.4	56.1
12-1	110	13.8	57.8

1. 100 grams lactose at 9 A.M.
2. Benedict's test weakly positive.
3. Benedict's test strongly positive.
4. 100 grams lactose at 8 A.M. No reduction test throughout.

Table XVII

Experiments 33 and 34 - Fats - Butter

200 cc water per hour

Experiment 33

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	49.0	21.8	57.7
7-8	210.0	20.1	54.6
8-9 ¹	156.0	18.1	54.9
9-10	265.0	21.0	60.9
10-11	112.0	24.8	57.1
11-12	288.0	16.4	54.1

Experiment 34

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	32	20.5	57.1
7-8	195	21.5	55.0
8-9 ²	78	19.0	57.7
9-10	156	21.0	58.0
10-11	182	25.1	60.6
11-12	49	12.8	53.8
12-1	70	15.8	60.3

1. 100 grams creamery butter at 8 A.M.

2. 100 grams creamery butter at 8 A.M.

Table XVIII

Experiments 35, 37, 38 and 40 - Glycerol

200 cc. water per hour

<u>Experiment 35</u>			<u>Experiment 37</u>	
<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Volume</u> cc	<u>Uric Acid</u> mg
6-7			37.5	14.1
7-8	23.5	18.9	254.0	19.9
8-9	28.5	26.9	103.0 ²	17.2
9-10	91.0 ¹	60.6	80.0	26.6
10-11	³		197.0	24.4
11-12	38.0	39.5	136.0	24.3
12-1	39.0	35.7	274.0	18.8
1-2	44.0	36.6		
2-3	122.0	17.4		

<u>Experiment 38</u>			<u>Experiment 40</u>	
<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Volume</u> cc	<u>Uric Acid</u> mg
6-7	87	14.3		
7-8	246	16.8	75	18.7
8-9	232 ⁴	16.0	240	20.6
9-10	98	21.9	286 ⁵	18.3
10-11	180	24.8	364	20.3
11-12	170	24.3	213	22.6
12-1			161	15.4

1. 50 grams glycerol at 9 A.M.
2. 50 grams glycerol at 8 A.M.
3. Two hour sample 9-11 A. M.
4. 50 grams glycerol at 8 A.M.
5. 10 grams glycerol at 9 A.M.

Table XIX

Experiments 25 and 26 - Exercise

200 cc. water per hour

Experiment 25

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
6-7	33	18.8	52.5
7-8	130	17.9	56.4
8-9	69	15.3	57.3

Experiment 26

<u>Hour</u>	<u>Volume</u> cc	<u>Uric Acid</u> mg	<u>Creatinine</u> mg
7-8	33	18.7	55.0
8-9	94	18.8	57.2
9-10	31	8.4	29.1
10-11	27	17.0	68.0
11-12	31.5	20.9	53.3
12-1	74	23.7	67.5

In experiment 25, some strenuous exercise consisting of basketball, track work and gymnastics was taken from 6-7 P.M. the preceding evening. This exercise left the subject exhausted.

In experiment 26, strenuous exercise similar to that in experiment 25 was taken from 6-7 P.M. the preceding evening and from 9-10 during the experimental day. Experiments 25 and 26 were carried out on two consecutive days.

B I B L I O G R A P H Y

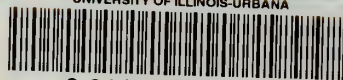
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